REMARKS

Claims 1-22, 25, 26, 32, 38 and 39 are pending.

The hypertext links have been deleted. Claims 38 and 39 are dependent from claims that have been withdrawn. Therefore, these claims are withdrawn also.

Claims 15 and 16 are objected to. The claims have been amended accordingly to depend from claim 8. Claims 1, 4, 6, 7, 12, 15, 21 and 32 have been additionally amended. Claims 2, 3 and 20 have been cancelled.

Support for the amendments are provided in the specification, for example, on pages 24, 26 and 27 and in the cancelled claims. No new subject matter is believed to be added.

The Examiner has objected to the claims as lacking enablement because the Examiner asserts no guidance is provided for the use of viroid RNA other than the Avocado sunblotch Viroid (pg. 3 of the office action) as a chloroplast localization sequence (CLS). However, a description is provided of at least 3 different viroids with CLS in the examples as well as a genus of viroids defined by their ability to replicate in the chloroplast. The ability of the viroid to replicate in the chloroplast was already established in the prior art at the time of filing the present application (see for example, Bussiere et al. (1999) copy attached hereto). A novel aspect of the claimed invention resides in the use of a cleavage-deficient viroid sequence containing a CLS fused to non-viroid RNA sequences.

A method of inactivating the self-cleaving property of a viroid sequence is described on page 27 and does not require undue experimentation where the state of knowledge in the art is at a high level (also, see Table 1 of the Waterhouse reference and Bussiere et al.).

The Examiner further asserts that with respect to contacting the chloroplast with RNA, the specification only describes how to transform plant cells with DNA. The Examiner further suggests that transformation of DNA into plant cells is sequence-dependent and that Applicants have only provided one sequence. However, DNA can be introduced into plant cells by any number of methods (see page 30).

Applicants have described how after the DNA is introduced into the cells, it is transcribed in the nucleus and the RNA is then transported into the chloroplast by way of a chaperone (CLS). The claims have been amended to more distinctly describe the invention.

The Examiner asserts that if the mechanism for translocation of RNA by viroids into a natural target site is unknown, then translocation itself is unpredictable. In support of this assertion, the Examiner cites the Okita and Croft references, which are reviews covering RNA localization as part of plant embryogenesis. The references do not appear to discuss the fate of RNA transcribed from externally introduced DNA nor do they refer to viroid RNA nor do they refer to chloroplast localization sequences in viroids. Embryogenesis may involve unpredictable mechanisms of translocation, but this does not

reflect on the predictability of RNA localization of viroid sequences.

The Examiner has rejected the claims as failing the written description requirement. In particular, the Examiner asserts that the biomolecular sequence is described only by a functional characteristic without any known or disclosed correlation between that function and the structure of the sequence and as such is not sufficient. In fact, viroid sequences of at least three representative members of those viroids that replicate in the chloroplast are readily available in public genome databases as evidenced by the attachment hereto. It is here asserted that a representative number of examples (three examples) provide an adequate description commensurate with the predictability of the art and the scope of the amended claims. Moreover, contrary to the Examiner's statement on page 7 of the office action, applicants have described how to transform plant cells with DNA (see for example, page 30 (5) "Introducing DNA fragments into targeted compartments within the host cells").

Rejection under 35 U.S.C. §102(e)

The Examiner rejects the claims as anticipated by Waterhouse et al. Waterhouse et al. describe a version of gene silencing using dsRNAs that bind to and degrade mRNA so as to reduce the expression of a targeted protein.

The abstract of the reference states: "methods are provided for reducing phenotypic expression of a nucleic acid of interest in plant cells" (emphasis added).

The reference in the abstract describes targeting target-specific RNA to the nucleus not the chloroplast and utilizes self-splicing ribozymes

The Examiner asserts that "translocation of the RNA transcribed to the chloroplast would be an inherent property of the transcribed RNA given the localization of avocado sunblotch viroid to the chloroplasts". However, there is no suggestion that the transcribed RNA was a cleavage-inactivated viroid sequence fused to another RNA sequence in a non-naturally occurring association. Indeed, the trans-splicing property of the ribozyme described in the reference results in cleavage at a site preceding the polyadenylation site to generate unpolyadenylated target specific RNA molecules for reducing phenotypic expression. This teaches away from the present claimed invention.

In summary, the present claimed invention in claims 1-14, 17-19, 20-21 and 25-26 differs from the reference in at least the following aspect, namely, that the present claimed invention relies on a CLS having substantial homology with a cleavage-inactivated viroid sequence or consisting of at least part of a chloroplast replicating cleavage-inactivated viroid sequence fused to a second non-viroid sequence.

Rejection under 35 U.SC. §103

The Examiner has rejected the claims as obvious in light of Waterhouse in view of Sanford et al. Applicants assert that

Waterhouse teaches away from the present claimed invention for the reasons provided above. The combination of Waterhouse with Sanford et al. does not suggest or teach the claimed invention.

CONCLUSION

Applicants respectfully submit that this case is in condition for immediate allowance. Early and favorable consideration leading to prompt issuance of this Application is earnestly solicited.

Applicants petition for a three-month extension of time and submit check in the amount of $510 to cover the petition fee. Applicants authorize that any deficiencies be charged to deposit account number 14-0740.

Respectfully submitted,

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Avocado sunblotch viroid, complete genome.
ACCESSION J02020
tttattagaa caagaagtga ggatatgatt aaactttgtt tgacgaaacc aggtctgttc
61 cgactttccg actctgagtt tcgacttgtg agagaaggag gagtcgtggt gaacttttat
121 taaaaaaatt agttcactcg tcttcaatct cttgatcact tcgtctcttc agggaaagat
181 gggaagaaca ctgatgagtc tcgcaaggtt tactcctcta tcttcattgt ttttttacaa
241 aatcttg

Peach latent mosaic viroid hammerhead structure RNA sequence.
ACCESSION M83545
1 gtcataagtt tcgtcgcatt tcagcgactc atcagtgggc ttagcccaga cttatgagag
61 agtaaagacc tctcagcccc tccaccttgg ggtgccctat tcggagcact gcagttcccg
121 atagaaaggc taagcacctc gcaatgaggt aaggtgggac ttttccttct ggaaccaagc
181 ggttggttcc gagggggggtg tgatccaggt accgccgtag aaactggatt acgacgtcta
241 cccgggattc aaacccgtcc cctccagaag tgattctgga tgaagagtct gtgctaagca
301 cactgacgag tctctgagat gagacgaaac tcttctt

Chrysanthemum chlorotic mottle viroid.
ACCESSION Y14700
1 ggcacctgac gtcggtgtcc tgatgaagat ccatgacagg atcgaaacct cttccagttt
61 cggcttgtgt gggagtaaag ctttcgctct ctccacagcc tcatcaggaa acccacttca
121 ggtctcgact ggaaggtcgt taaacttccc ctctaagcgg agtagaggta aatacctccg
181 tccaaccccg ggaggaaagg ggttgggacc cggaacagat ccagttccgg tcctttggag
241 tccatttctc tcgttggata ttctcctcgg agaagggaga tggggccagt cccagtcggt
301 tcgctctcgt agtcacagcc actggggaac ctaggcagat ggctggacgg agtcttagtc
361 cactccagag gaccttgggt ttgaaacccc caagaggtc